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Medicine

A CASE REPORT OF ACROMEGALY

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ABSTRACT Acromegaly is a disorder related to excessive production of growth hormone and characterized by progressive somatic disproportional growth. It is most often diagnosed in adults in third to fourth decade of life. The main clinical features are broadened extremities hands and feet, widened thickened fingers, and thickened soft tissue. Patients have coarse facies with widened and thickened nose, prominent cheekbones, prominent forehead, thick lips and marked facial lines. Mandibular overgrowth is observed causing prognathism and teeth are widely spaced. The disease also has cardiovascular, respiratory, rheumatologic and metabolic consequences which determine its prognosis. The clinical diagnosis is confirmed biochemically by an increased serum GH following OGTT and insulin-like growth factor-I. Treatment is aimed at correcting or preventing tumour compression by excising the disease-causing lesion, and at reducing GH and IGF-I levels to normal values. First-line of treatment is transsphenoidal surgery. When surgery fails, medical treatment and/or radiotherapy can be used.

KEYWORDS : Pituitary macroadenoma ; Acromegaly

52 years old male patient, resident of Pune, labourer by occupation, presented with chief complaints of Headache since 4 – 5 months; Increased thirst for 5 days; Increased urination since 5 days. Patient was apparently alright about 4-5 months back when he started experiencing HEADACHE; which was bilateral, frontal, throbbing, relieved by sleep and medicines with no h/o (history of) photophobia / nausea / fever. He also started experiencing excessive thirst since 10 days, which made him to drink seven to eight litres of water in a day. Subsequently he started having polyurea; frequent urination since last 10 days.

He was Known case of hypertension since last 9 years on regular treatment. He was having normal facial features till the age of 25 years after which his facial features gradually enlarged disproportionately, with enlarged nose, ears, lips with protrusion of the lower jaw. Also the size of the fingers of hand and shoe size increased over the period of time. No h/o Ischemic heart disease / Stroke / Tuberculosis On further enquiry he also h/o snoring and disturbed sleep at night and day time sleepiness.

He was having reduced sleep and appetite since few years. He was chronic alcoholic / smoker / tobacco chewer since 20 years. He was having increased thirst and increased urination since last months.

On examination Patient was conscious, oriented, cooperative, sitting comfortably on the bed. Vitals were normal i.e. Pulse 88 bpm, blood pressure 130/80 mmHg (on both arm), Respiratory rate 18 /min, SPO2 98%, there was no Pallor / Icterus / Cyanosis. body mass index was 30.47 kg/sq.m. Enlarged nose, lips, tongue with coarse facies was present were present. Lower jaw was protruded (Prognathism +). Macroglossia Broadened fingers Thickened heels and broad feet. Fingers and toes were increased in size and broadened and soles were thickened. Systemic examination was within normal limits.

Figure 1: Broadened fingers

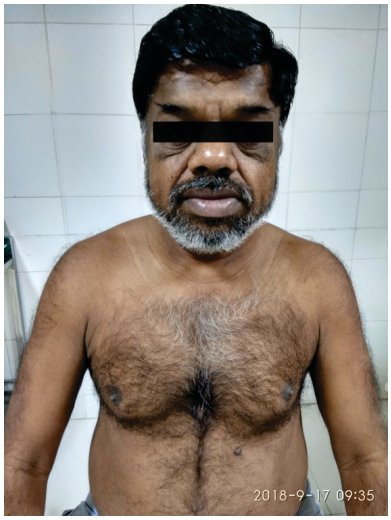

Figure 2: Enlarged nose, lips, tongue with coarse facies

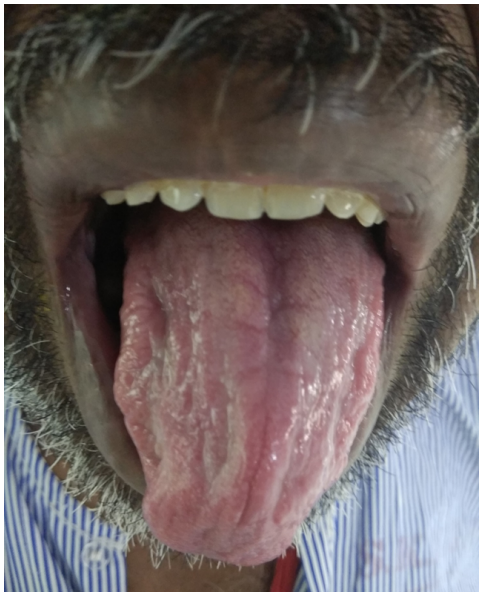

Figure 3: enlarged tongue with macroglossia

Primary investigations were within normal limits. (Hb14.56; TLC 6200; PLT 2 L; RBSL 115 mg/dl; Urea 10 mg/dl; Creatinine 0.6 mg/dl; Na 135 / K 3.5 / Cl 98; Bilirubin (T/D) 1.3 / 0.5 (mg/dl); Urine=normal.

Abdominal sonography was suggestive of mild hepatomegaly with fatty infiltration. 2D Echo was normal. There was increased heal pad thickness on x ray of foot. bilateral perimetry showed ring scotoma with clover leaf pattern, fundus examination was normal.

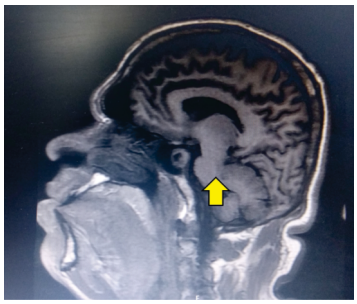

Figure 4: MRI brain was suggestive of pituitary macroadenoma with cystic degeneration focus in anterior pituitary

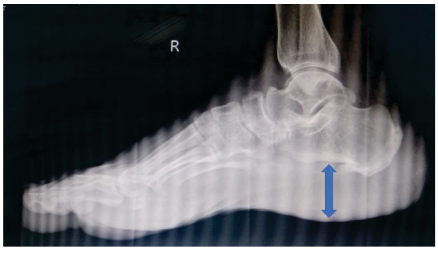

Figure 5: Increased heel pad thickness (30mm) on X ray foot lateral view

We suspected diagnosis of acromegaly and sent serum Growth Hormone (GH) levelswhich were found to be 12.7 ng/ml and serum IGF level were found to be 920.00 ng/ml. We also did measure other pituitary hormone levels, 8 am Sr. Cortisol was found to be <1.0 ug/ml (decreased). Sr. Prolactin and Sr. Parathyroid Hormone (PTH) were found in normal limits. MRI (Magnetic Resonance Imaging) brain was suggestive of pituitary macroadenoma with cystic degeneration focus in anterior pituitary. Neurosurgeon opinion was taken and we decided to go ahead with surgical excision of macroadenoma. Thereafter he underwent successful surgical removal of macroadenoma through transsphenoidal route. Recovery was excellent.

DISCUSSION:

Acromegaly is characterized by an acquired progressive somatic disfigurement, mainly involving the face and extremities, but also many other organs, that is associated with systemic manifestations.(Bonadonna, Doga, Gola, Mazziotti, & Giustina, 2005) The disease is related to the excessive production of growth hormone (GH). This GH hypersecretion originates from a monoclonal benign pituitary tumour (adenoma) in more than 90% of cases.(Chanson & Salenave, 2008)

Dysregulated growth hormone (GH) hypersecretion is usually caused by a GH-secreting pituitary adenoma and leads to acromegaly — a disorder of disproportionate skeletal, tissue, and organ growth.(Katznelson et al., 2014)

If the condition is untreated, enhanced mortality due to cardiovascular, cerebrovascular, and pulmonary dysfunction is associated with decrease in lifespan.(Giustina et al., 2003)

Primary Work up in ACROMEGALY
- Sr GH levels
- Oral Glucose Tolerance Test
- Sr IGF-1 levels
- MRI Brain (Plain + Contrast)

SERUM GH LEVELS

The diagnosis of acromegaly requires demonstration of dysregulated and enhanced GH secretion. Accordingly, a random GH value of less than 0.04µg/l effectively excludes the diagnosis of acromegaly.

Even newer immunoradiometric assays have challenges of reproducibility, lack of universal standards, nonuniform antibody recognition of GH isoforms, and the presence of circulating GH-binding proteins.

ORAL GLUCOSE TOLERANCE TEST (OGTT)

HALLMARK of ACOMEGALY: Inability to respond appropriately to a glucose-induced neuroendocrine suppressive signal

The inability to suppress GH secretion to less than 1µg/l during 2 hours after an oral glucose load (75 grams) is the current consensus for diagnosing acromegaly.

However, this cutoff may in fact be insensitive. Failure to suppress GH levels- in diabetes / renal or hepatic failure / obesity / those receiving estrogen replacement or / pregnant.

Serum IGF1

Screening of IGF1 levels is useful in obtaining a surrogate reflection of integrated GH secretion. IGF1 levels are relatively stable, correlate with clinical features of acromegaly.

Malnourished patients and those with liver and renal failure or those receiving estrogen exhibit lower IGF1 levels.

MRI Brain (Plain and Contrast)

Other Pituitary Hormones

COMORBIDITIES IN ACROMEGALY

- hypertension
- cardiac arrhythmias
- glucose intolerance and
- diastolic dysfunction leads to heart failure; which may be intractable, especially if GH levels remain uncontrolled

Biventricular cardiac hypertrophy manifests early in response to elevated GH levels and is independent of the presence of hypertension.(Pivonello et al., 2017)

Post exercise ventricular ejection fraction is increased in approximately 70% of patients and approximately 50% are at intermediate-to-high risk for coronary arteriosclerosis.

The pathogenesis of hypertension is associated with plasma volume expansion and increased cardiac output.

GH exerts anti natriuretic effects, leading to increased extracellular volume, soft tissue swelling, and organomegaly.

GH acts at the aldosterone-sensitive distal nephron causing sodium retention.

Insulin resistance caused by GH excess results in glucose intolerance and diabetes, further exacerbating renal dysfunction.(Adelman, Liebert, Nachtigall, Lamerson, & Bakker, 2013)

Airway obstruction consequent to macroglossia (tongue enlargement) and hypertrophy of laryngeal and pharyngeal mucosal tissues lead to upper airway obstruction, hypoventilation, snoring, and sleep apnea in approximately 50% of patients.

The goals of acromegaly management–(Dineen, Stewart, & Sherlock, 2016)
- Control of GH and IGF1 secretion and tumor growth
- Relief of compressive effects on CNS and vascular structures
- Preservation or restoration of pituitary hormone reserve function
- Treatment of comorbidities and normalization of mortality rates.

Surgery

Surgery is technically challenging due to anatomic inaccessibility of the pituitary gland; Functioning tumor microfoci often invade Dural spaces; cavernous sinus are not readily visible at surgery; and tumor can continue to secrete GH after tumor resection. Over 90% of resections are performed via an endonasal transsphenoidal approach, often with minimally invasive endoscopic techniques.(Melmed et al., 2009)

Computerized image guidance and intraoperative MRI coupled with development of micro instrumentation and optics have resulted in safe, effective, and minimally traumatic procedures.

The goal of surgery is to balance maximal tumor mass resection with preservation of normal pituitary secretory function.

About 70% of patients harboring well-circumscribed GH-secreting microadenomas less than 10 mm in diameter achieve long term biochemical control after surgery.

Surveillance for pituitary function (including thyroid function and gonadotropins-secreting function) is recommended at 6—12 weeks after surgery to assess whether hormone replacement therapy is needed. Follow-up MRI of the brain is recommended in at least 12 weeks after surgery. Medical therapy is indicated for all patients who did not achieve clinical and biochemical disease control after incomplete tumor resection.'"(Astafeva, Kalinin, & Kadashev, 2017)

Radiotherapy

Conventional external-beam radiotherapy is administered up to a maximum of 4000–5000 cGy in 180-cGy weekly doses spread over six weeks.

Overall, about 50% of patients achieve biochemical remission (GH < 2 μg/l and normalized IGF1) after 10 years.

The relatively long latency period required to achieve remission is a major disadvantage.

Stereotactic radiosurgery

Using a Cobalt60 source, relatively narrow beams of high-dose, focused γ radiation are delivered with stereotactic precision to a small tumor, and the approach is particularly effective in tumors less than 3 cm in diameter and distant from the optic tract.

Five years after treatment, post-OGTT serum GH levels are less than 1 μg/l in approximately 50% of patients.

SSTR ligands

Octreotide s.c. or i.v. injection. Octreotide binds avidly to SSTR2 and to a lesser extent to SSTR5. The starting dose is 100–250 μg every 8 hours, and up to 1.5 mg/24 hours can be safely administered in patients with acromegaly . Half-life of octreotide is up to 2 hours

The long-acting release (LAR) intramuscular formulation is encapsulated within biodegradable D, l-lactic, and glycolic acid copolymer microspheres. The starting dose is usually 20 mg every 28 days, with safe maximal monthly doses up to approximately 60 mg or higher. Drug levels peak at 28 days, and plateau concentrations are sustained for approximately 14 days.(Melmed et al., 2009)

Lanreotide is incorporated into a biodegradable polymer for intramuscular injection (30 or 60 mg) every 7–14 days. With an approximately five-day half-life, the molecule exhibits high SSTR2 affinity and also binds less avidly to SSTR5. Newer SRL molecules like pasireotide binds with high affinity to SSTR1, SSTR2, SSTR3, and SSTR5. The molecule is currently being evaluated for treatment of octreotide-resistant GH-secreting adenomas.(Gadelha, Wildemberg, Bronstein, Gatto, & Ferone, 2017)

GH Receptor antagonist

Pegvisomant is the drug abrogates GHR signalling and is pegylated to generate a stable molecule The drug thus blocks IGF1 generation by specifically antagonizing peripheral GH action. Patients receiving daily pegvisomant doses of 10–30 mg, about 70% achieved normal IGF1 levels after 24 months.(Giustina et al., 2017)

REFERENCES

1. Adelman, D. T., Liebert, K. J., Nachtigall, L. B., Lamerson, M., & Bakker, B. (2013). Acromegaly: the disease, its impact on patients, and managing the burden of long-term treatment. International Journal of General Medicine, 6, 31–38. https://doi. org/ 10.2147/IJGM.S38594
2. Astaf'eva, L. I., Kalinin, P. L., & Kadashev, B. A. (2017). Modern diagnosis and postoperative monitoring of acromegaly patients at a neurosurgical clinic. Voprosy Neirokhirurgii Imeni N.N. Burdenko, 81(1), 58. https:// doi. org/ 10.17116/ neiro201780758-62
3. Bonadonna, S., Doga, M., Gola, M., Mazziotti, G., & Giustina, A. (2005). Diagnosis and treatment of acromegaly and its complications: consensus guidelines. Journal of Endocrinological Investigation, 28(11 Suppl International), 43–47. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/16625844
4. Chanson, P., & Salenave, S. (2008). Acromegaly. Orphanet Journal of Rare Diseases, 3(1), 17. https://doi.org/10.1186/1750-1172-3-17
5. Dineen, R., Stewart, P. M., & Sherlock, M. (2016). Acromegaly – Diagnosis and Clinical Management. QJM, hcw004. https://doi.org/10.1093/qjmed/hcw004
6. Gadelha, M. R., Wildemberg, L. E., Bronstein, M. D., Gatto, F., & Ferone, D. (2017). Somatostatin receptor ligands in the treatment of acromegaly. Pituitary, 20(1), 100–108. https://doi.org/10.1007/s11102-017-0791-0
7. Giustina, A., Arnaldi, G., Bogazzi, F., Cannavò, S., Colao, A., De Marinis, L., … Ghigo, E. (2017). Pegvisomant in acromegaly: an update. Journal of Endocrinological Investigation, 40(6), 577–589. https://doi.org/10.1007/s40618-017-0614-1
8. Giustina, A., Casanueva, F. F., Cavagnini, F., Chanson, P., Clemmons, D., Frohman, L. A., … Pituitary Society and the European Neuroendocrine Association. (2003). Diagnosis and treatment of acromegaly complications. Journal of Endocrinological Investigation, 26(12), 1242–1247. Retrieved from http:// www.ncbi. nlm.nih. gov/pubmed/15055479
9. Katznelson, L., Laws, E. R., Melmed, S., Molitch, M. E., Murad, M. H., Utz, A., & Wass, J. A. H. (2014). Acromegaly: An Endocrine Society Clinical Practice Guideline. The Journal of Clinical Endocrinology & Metabolism, 99(11), 3933–3951. https://doi.org/10.1210/jc.2014-2700
10. Melmed, S., Colao, A., Barkan, A., Molitch, M., Grossman, A. B., Kleinberg, D., … Giustina, A. (2009). Guidelines for Acromegaly Management: An Update. The Journal of Clinical Endocrinology & Metabolism, 94(5), 1509–1517. https:// doi.org/10.1210/jc.2008-2421
11. Pivonello, R., Auriemma, R. S., Grasso, L. F. S., Pivonello, C., Simeoli, C., Patalano, R., … Colao, A. (2017). Complications of acromegaly: cardiovascular, respiratory and metabolic comorbidities. Pituitary, 20(1), 46–62. https://doi.org/10.1007/s11102-017-0797-7